



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁶ :		A1	(11) International Publication Number: WO 97/07214																								
C12N 15/16, C07K 14/575, 7/06, 7/08, 16/26, A61K 38/08, 38/10, 38/22, 39/395, G01N 33/53, C12Q 1/68			(43) International Publication Date: 27 February 1997 (27.02.97)																								
(21) International Application Number: PCT/US96/13286																											
(22) International Filing Date: 16 August 1996 (16.08.96)																											
(30) Priority Data:																											
60/002,514	18 August 1995 (18.08.95)	US	21710 (US). MARTINEZ, Alfredo [US/US]; 1231 Otis Street, N.E., Washington, DC 20017 (US). MILLER, Mae, Jean [US/US]; 4013 Middleton Drive, Monrovia, MD 20850 (US). UNSWORTH, Edward, J. [US/US]; 4414 Glenridge Street, Kensington, MD 20895 (US). HOOK, William [US/US]; 4008 Jeffry Street, Wheaton, MD 20906 (US). WALSH, Thomas [US/US]; 6006 Roosevelt Street, Bethesda, MD 20817 (US). GRAY, Karen [US/US]; 18700 Walkers Choice Drive, Gaithersburg, MD 20879 (US). MACRI, Charles [US/US]; 3302 Saul Road, Kensington, MD 20895 (US).																								
60/002,936	30 August 1995 (30.08.95)	US																									
60/013,172	12 March 1996 (12.03.96)	US																									
(60) Parent Application or Grant																											
(63) Related by Continuation																											
US	60/013,172 (CIP)																										
Filed on	12 March 1996 (12.03.96)																										
(71) Applicant (for all designated States except US): THE GOVERNMENT OF THE UNITED STATES OF AMERICA, represented by THE SECRETARY, DEPARTMENT OF HEALTH AND HUMAN SERVICES [US/US]; Office of Technology Transfer, National Institutes of Health, Suite 325, 6011 Executive Boulevard, Rockville, MD 20852 (US).																											
(72) Inventors; and																											
(75) Inventors/Applicants (for US only): CUTTITTA, Frank [US/US]; 7908 Hope Valley Court, Adamstown, MD																											
(54) Title: FUNCTIONAL ROLE OF ADRENOMEDULLIN (AM) AND THE GENE-RELATED PRODUCT (PAMP) IN HUMAN PATHOLOGY AND PHYSIOLOGY																											
(57) Abstract																											
<p>The methods of the present invention demonstrate that adrenomedullin (AM) is expressed in human cancer cell lines of diverse origin and functions as a universal autocrine growth factor driving neoplastic proliferation. The present invention provides for AM peptides and AM antibodies useful in therapeutic, pharmacologic and physiologic compositions. The present invention additionally provides for methods of diagnosis, treatment and prevention of disease utilizing compositions comprising the AM peptides and antibodies of the present invention. The methods of the present invention also provide for experimental models for use in identifying the role of AM in pancreatic physiology. The methods pertaining to rat isolated islets have shown that AM inhibits insulin secretion in a dose-dependent manner. The monoclonal antibody MoAb-G6, which neutralizes AM bioactivity, was shown by the methods of the present invention to increase insulin release fivefold, an effect that was reversed by the addition of synthetic AM.</p>																											
<p style="text-align: right;">Peptide</p> <table border="1"> <caption>Data extracted from the bar chart (% Inhibition of Growth vs Peptide concentration)</caption> <thead> <tr> <th>Peptide Concentration (nM)</th> <th>Peptide 1 (%)</th> <th>Peptide 2 (%)</th> </tr> </thead> <tbody> <tr><td>0</td><td>0</td><td>0</td></tr> <tr><td>1</td><td>~45</td><td>~15</td></tr> <tr><td>10</td><td>~65</td><td>~15</td></tr> <tr><td>100</td><td>~75</td><td>~15</td></tr> <tr><td>1000</td><td>~65</td><td>~15</td></tr> <tr><td>10000</td><td>~55</td><td>~15</td></tr> <tr><td>100000</td><td>~45</td><td>~15</td></tr> </tbody> </table>				Peptide Concentration (nM)	Peptide 1 (%)	Peptide 2 (%)	0	0	0	1	~45	~15	10	~65	~15	100	~75	~15	1000	~65	~15	10000	~55	~15	100000	~45	~15
Peptide Concentration (nM)	Peptide 1 (%)	Peptide 2 (%)																									
0	0	0																									
1	~45	~15																									
10	~65	~15																									
100	~75	~15																									
1000	~65	~15																									
10000	~55	~15																									
100000	~45	~15																									

